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Botulism

—Diagnosis, Management and Public Health Considerations

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Botulism is an uncommon but often fatal disease associated with ingestion of a potent neurotoxin present in improperly preserved foods. Exposures to commercially preserved foods with an odd or peculiar taste almost never represent exposure to botulism toxin. Improperly prepared home-canned products which are tasted or consumed without heating are more likely to be associated with botulism.

The management of suspect and confirmed cases of botulism is presented by medical epidemiologists in the State Department of Public Health, Bureau of Communicable Disease Control, to provide physicians in California with a practical approach to this problem.

BOTULISM is an uncommon but often fatal illness due to a potent neurotoxin produced by Clostridium botulinum. Spores of C. botulinum are ubiquitous but are not in themselves dangerous when ingested; however, the toxin may be elaborated when spores germinate in an anaerobic environment. Botulinum *toxin* is readily destroyed by boiling but some types of botulinum *spores* are not. Therefore, pressure cooking to reach temperatures of 240°F may be necessary to destroy all C. botulinum spores in certain foods. If some spores survive and germinate, toxin may be elaborated during storage. Disease is usually due to ingestion of preformed toxin in improperly preserved vegetables, fruits, meat or fish products. Botulism has also resulted from wounds infected with C. botulinum in which toxin is produced *in vivo*. Six toxigenic types of C. botulinum are recognized—types. A, B, C, D, E, F. Botulism in humans is almost always caused by A, B or E toxins, and very rarely F. Although types C and D cause botulism in some animal species, these toxin types do not cause disease in humans, with possible rare exceptions.[1]

A recent publication[2] shows that between 1899 and 1969, there have been 659 outbreaks of botulism comprising 1,696 cases. A total of 234 (34 percent) of the outbreaks were reported from California. The reasons for this disproportionate percentage for California's population are speculative, and may include a greater awareness of botulism due to Meyer's work[3] or perhaps a greater concentration of botulism spores in California soil than elsewhere. Type A botulism has accounted for 72 percent of typed outbreaks nationally; in California, type A accounted for 87 percent, B for 7 percent, E for 1 percent, F for 1 percent, and A and B together for 3 percent. The state's only documented type E outbreak occurred in 1941 and was traced to imported commercially grown mushrooms canned in San Francisco.[4] The nation's only

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type F outbreak occurred in California and was traced to home-prepared venison jerky.[5]

The botulism case fatality rate has decreased in recent years. Nationally, it was 60 percent between 1899 and 1949, but less than 30 percent between 1960 and 1969.[2] The incidence of botulism has also decreased since 1940.[2] As a result of high and improving standards in the canning industry, this disease is much less frequently due to commercial foods than it was in earlier years. In the United States between 1960 and 1969, ten outbreaks of botulism associated with commercially processed foods were reported; these represented only 13 percent of all outbreaks of botulism during that period. Most of the outbreaks from commercial foods since 1960 were due to improperly preserved—not canned—fish or meat products. California's cases of botulism have been due primarily to faultily home-canned or preserved vegetables. See Table 1.

TABLE 1.—*Botulism Cases by Source California, 1950-1971*

	Cases
Food, Home Processed	
Fruits and Vegetables*	74
Tuna	4
Deer Jerky	3
Pickled Pigs Feet	1
TOTAL	82
Food, Commercially Processed	
Cheese	1
Chopped Chicken Liver	1
TOTAL	2
Wound Infection	4
Unknown	8
TOTAL CASES	96

*Includes mushrooms 15, olives 7, chili peppers and beans 16, fruits and fruit juices 7, tomatoes 4, figs 4, okra 2, corn 1, stringbeans 2, cactus 2, beets 1, par par 3, avocado sauce 1, choyote 1, potatoes 1, black-eye peas 3, squash 1, "vegetables" unspecified 1, "Korean vegetable dish" 2.

SOURCE: State of California, Department of Public Health, Morbidity Records.

Diagnosis

Clinical Presentation

Incubation periods reported in the literature range from six hours to eight days, with an average of 12 to 36 hours. In recent years the extremes have not been encountered in California and most cases had incubation periods of 12 to 48 hours.

Presenting complaints generally consist of: (1) ptosis, (2) blurred or double vision, and/or (3) dry, sore throat; sometimes all three. In the 1971 Bakersfield outbreak[6] involving five cases, several persons presented with sore throat as their chief but not sole complaint.

Vital signs (blood pressure, temperature, pulse, respiration) are remarkable for their normality when patients are first seen, though postural hypotension may sometimes be exhibited. Fever is conspicuously absent unless secondary complications such as pneumonia or urinary tract infection supervene. Arrhythmias occasionally occur, but they have not been observed as a prominent part of the clinical picture. Respiratory difficulty is not usually present with initial symptoms.

Neurologic factors. Weakness or paralysis in botulism is most frequently of the descending type. Paralysis is usually but not always symmetrical. There is early ptosis and eye muscle involvement, with limited motion of extraocular muscles, strabismus, and nystagmus on testing. Pupils may be fixed and dilated. There may be dizziness, facial paralysis, dysphonia, dysphagia, and inability of the neck muscles to support the head. Disease may progress to quadriplegia and respiratory failure, but no patient developed respiratory symptoms to our knowledge without first having cranial nerve deficits, nor has respiratory difficulty been a sudden development.

Deep tendon reflexes are frequently depressed symmetrically, or absent. Conspicuously absent is any objective sensory disturbance despite profound motor abnormalities that may be in evidence. Paresthesia and decreased tactile perception are not part of the neurologic picture of botulism, nor is there any subjective discomfort (pain, tenderness) at paralyzed areas. Abdominal pain due to paralytic ileus may develop, with attendant constipation. Headache and retrosternal burning have been reported, but the pain we have most commonly noted in botulism is that associated with the pharyngitis mentioned earlier. In conjunction with this symptom, mucous membranes of the mouth and pharynx are found to be dry and erythematous. In some cases botulism has been initially misdiagnosed and treated as "strep throat."

Despite the *appearance* of lethargy given by ptosis, flexed neck while sitting, and difficulty in communicating verbally, the toxin does not affect the sensorium; mental clarity remains intact in botulism unless complications develop. Only rarely do patients with botulism have gastrointestinal symptoms of nausea, vomiting, abdominal cramps or diarrhea; these are, however, more likely to occur with type E botulism than with types A and B.

TABLE 2.—*Paralytic Diseases Confused with Botulism*

Disease	*Features distinguishing this disease from botulism*
Cerebrovascular accident involving midbrain	Localized signs, sensory deficits, asymmetric deep tendon reflexes
Polio and other encephalitides	Fever, altered mental state, abnormal CSF
Guillain-Barré syndrome	Ascending paralysis, paresthesia, pain, abnormal CSF
Myasthenia gravis	Muscular fatiguability, positive Tensilon test
Tick paralysis	Presence of a tick, paresthesia of affected extremities
Paralytic shellfish poisoning	Incubation period 15-60 minutes, paresthesia
Carbon monoxide poisoning	Altered mental state, cherry-colored skin
Organic phosphate poisoning	Fever, altered mental state, miosis, increased oral and respiratory secretions, fasciculations, muscle cramps, paresthesia, depressed serum cholinesterase
Antibiotic paralysis (kanamycin, streptomycin, neomycin, etc.)	Secondary to antibiotics administered under general anesthesia
Poisoning with belladonna-like alkaloids	Fever, tachycardia, altered mental state

Laboratory Studies

An attempt should be made to confirm suspicion of botulism by demonstrating that the patient's serum is toxic for mice. Before botulism antitoxin is administered, at least 10 ml of serum should be collected and refrigerated until delivered to the laboratory. Preliminary test results are usually not available for 24 hours and cannot be used initially to decide whether or not to administer antitoxin. If treatment is clinically indicated, antitoxin should be administered without delay.

Type A toxin may not be detected sometimes even when serum is collected early, possibly because of its rapid removal from circulation and early fixation to nerve tissue.[7] Type E and B toxins can circulate for much longer periods; they have been detected in serum as long as 10 and 22 days, respectively, after ingestion.[7] In situations involving clinically suspect botulism, suspect food(s) and their containers—even when empty—should be collected immediately, refrigerated, and tested for botulism toxin as soon as possible. In situations where only possible exposure to botulism is considered, toxicity testing of commercial food is usually not indicated (see public health management, below).

Cultures of stool specimens are not worthwhile. Clostridium botulinum is rarely isolated; when it is, its relevance to the problem is questionable. Necropsy studies have revealed no specific histopathologic appearance of nerve tissue or other tissues.

Routine laboratory studies including complete blood count, sedimentation rates, and blood chemical determinations are not helpful in the diagnosis of botulism. Urinalysis has, at times, shown proteinuria but this finding is nonspecific. Studies of cerebrospinal fluid are remarkable in being within normal limits. Chest x-ray films may show elevation of the diaphragm secondary to diaphragmatic paresis and atelectasis. Electrocardiograms may show nonspecific ST-T wave abnormalities, bundle branch blocks or arrhythmias.

Differential Diagnosis

Diseases which may cause acute paralytic illness are frequently confused with botulism: Guillain-Barré syndrome, carbon monoxide poisoning, encephalitis, myasthenia gravis, and cerebrovascular accidents are the most common. These and other diseases may be distinguished from botulism by key features noted in Table 2, which incorporates the most likely paralytic diseases encountered in a differential diagnosis. References should be consulted for detailed descriptions of these and other conditions.

Management

Public Health Management

Suspect cases of botulism, and cases of exposure to suspicious foods, should be reported to the local health department immediately. Prompt investigation is necessary to determine whether botulism is a possible problem so that suspect foods can be identified and eliminated as a continuing hazard. Health department staff will attempt to contact all persons known or suspected of having been exposed, to obtain detailed food histories and refer them for medical care. In addition, health department personnel will search the home or other sites of probable exposure to recover suspect foods and containers for appropriate laboratory study.

Clinical Management

The asymptomatic case with questionable exposure. Concern about botulism generally arises when an individual reports tasting or consuming a commercially canned food from a can that was bulging or whose contents tasted peculiar. Such bulging often represents an overfilled can, and detailed questioning frequently reveals that the

"explosion" on opening such cans is of fluid under pressure, not gas. Even when the cans are gaseous, the gas may merely be the result of chemical reactions subsequent to de-tinning of the can lining. Where foods are boiled before consumption, exposure to botulism toxin can be ruled out since the toxin is heat-labile. However, if such foods are not heated before ingestion, then potential for disease exists if toxin was present.

While these experiences with commercially canned foods almost never represent exposure to botulism toxin, it is advisable nonetheless to recommend evacuation of gastrointestinal contents as a precautionary measure. Vomiting should be induced or aspiration and lavage performed. A cathartic should be administered, and possibly an enema, too. As botulism toxin, once formed, is less stable at alkaline pH, it would appear reasonable to lavage with $NaHCO_3$. The administration of botulinum antitoxin carries some risk, and so its use is not advised in situations of questionable exposure. The patient may be followed as an outpatient under close medical observation. Such patients have generally not had exposure to botulism, and almost invariably no further action is necessary.

The asymptomatic case with probable exposure to botulism. This situation generally arises in a setting in which clinical cases of botulism are known to exist and where an asymptomatic person is suspected of having consumed the same incriminated food or meal. Asymptomatic patients in such a situation should be put into hospital for closer medical observation, and gastrointestinal contents should be evacuated as outlined in the section above. Serum should be obtained for mouse toxicity studies. The decision, however, to administer botulinum antitoxin to asymptomatic persons should be weighed carefully against the risks of potential anaphylaxis and serum sickness. Intensive observation may well be the safer course. However, at the first indication of possible symptoms of botulism, prompt treatment with antitoxin should be initiated.

The symptomatic case with suspected botulism. Admission to hospital, evacuation of toxin and antitoxin treatment.

On suspicion that a patient has developed signs and symptoms of botulism, it is imperative that he be put into hospital immediately—preferably in an intensive care unit. Efforts at eliminating toxin from the gastrointestinal tract should be undertaken as prescribed above. Pre-treatment serum should be obtained for mouse toxicity studies. Skin test for sensitivity to horse serum should be done as indicated on package inserts, then botulinum antitoxin administered promptly. If sensitivity to to horse serum is demonstrated, desensitization should be carried out according to instructions on the package insert. The earlier the initiation of antitoxin treatment, the better the prognosis.

Approximately 98 percent of typed botulism outbreaks in California since 1899 were type A, type B or both. Therefore, bivalent (AB) antitoxin will ordinarily be appropriate. Bivalent antitoxin is commercially available in California only from Lederle Laboratories in Los Angeles, phone (213) 723-6411 or (213) 722-3822. Trivalent (ABE) antitoxin, produced by Connaught Laboratories in Canada, is available from the Center for Disease Control, Atlanta, Georgia. An emergency supply of this antitoxin is kept at the State Health Department in Berkeley, phone (415) 843-7900. Trivalent antitoxin, because it includes type E antitoxin, is preferable until toxin type is determined. Type E antitoxin is especially important when the peccant food is from out-of-state—particularly fish from the Great Lakes area, Alaska or Japan. In California, the first dose of antitoxin may be either AB or ABE, depending on availability; subsequent doses of antitoxin ideally should be trivalent (ABE) unless laboratory results indicate A or B toxin, in which case the bivalent antitoxin can be used.

The potency of Connaught's 8 ml vial of ABE antitoxin in international units is A 7500, B 5500, E 8500; Lederle's 30 ml vial of AB antitoxin has A 10,000 and B 10,000. We recommend treating clinical cases with intravenous antitoxin, one vial every four hours until a total of four or five vials of ABE antitoxin or three or four vials of AB antitoxin has been administered. The antitoxin will bind circulating toxin and thereby prevent progression of neurologic symptoms, but it cannot undo paralysis already present. Serum may be tested subsequently for circulating toxin, and if toxin is detected additional antitoxin should be given. We have not observed persistence of circulating toxin in persons so treated. Follow-up testing for circulating toxin should be mandatory in cases of wound botulism to rule out continued elaboration of toxin in infected wounds.

If patients with botulism are first seen several days after onset of symptoms and there has been no progression at all of signs or symptoms in the preceding day or two, the administration of anti-

toxin may have little value, particularly when type A toxin is involved.

Guanidine hydrochloride—a drug currently under investigation—has been used to treat botulism. The similarity between the neuromuscular blocks of botulism and the Lambert-Eaton syndrome (for which guanidine has been of clinical value) prompted Cherington and Ryan[8,9,10] to investigate guanidine therapy for botulism. While they described favorable clinical responses such as increased vital capacity and improved extraocular movements following its use, a more recent study did not show any clinical benefit from guanidine.[11] Its role as an adjunctive measure in the treatment of botulism needs further study.

Attention to respiratory function has been at least as important as antitoxin therapy in reducing the case fatality rate in recent years. The immediate danger to the patient with botulism is respiratory insufficiency.[12] Accordingly, some feel that "early elective tracheostomy is mandatory."[13] However, since respiratory difficulty does not develop abruptly, it appears more reasonable to delay intubation until there are signs of impending respiratory difficulty. Even then, endotracheal intubation may be sufficient in mild cases, and safer when employed for no more than one week. In view of frequent complications (such as hemorrhage and infection) when tracheostomies are performed in hospitals with limited facilities and staff, serious consideration should be given to the possibility of transferring the patient immediately to a center proficient at inhalation therapy and intensive nursing care.

Respiratory function should be monitored by measurements of vital capacity and arterial blood gases. Pulmonary consultation should be obtained as soon as possible. If it appears that respiratory assistance will be needed, mechanical respiration with a tank respirator, an intermittent positive pressure breathing apparatus, or a volume respirator should be considered.

Inhalation therapists, physical therapists, chest physiotherapists and intensive nursing care play paramount roles in continuing clinical management. Frequent aseptic tracheal suctioning with disposable catheters, adequate humidification of inspired gases, attention to postural drainage, and continuous ventilatory support may prevent the occurrence of pneumonia. (Pneumonia developed in more than 50 percent of botulism patients with tracheostomy seen in California in the past several years.) If the patient's pulmonary function can be satisfactorily maintained and he can be kept alive, full neurologic recovery can be expected, although it may take months.

Ancillary Measures. On admission, a base-line electrocardiogram should be taken in all cases. Cardiac monitoring should be considered, and certainly it should be employed when heart block or an irregular rhythm is present. Urinary retention is a frequent occurrence, but it is best to wait until the need is demonstrated before insertion of an indwelling catheter. Even then, suprapubic cystostomy may be preferred. Antibiotic therapy should be reserved until development of such complications as respiratory or urinary tract infections. To prevent pulmonary aspiration, the patient should receive nothing by mouth until pharyngeal paralysis disappears. If aspiration of oral or gastric contents occurs, penicillin should be instituted immediately. Corticosteroids should also be given if less than 24 hours have intervened since aspiration of gastric contents in order to suppress pulmonary inflammatory reaction. The prolonged adynamic ileus sometimes seen in botulism may necessitate hyperalimentation infusions, via a central venous cannula, until bowel sounds return and nasogastric tube feedings can be instituted. Alternatively, a temporary feeding gastrostomy may be considered if bowel sounds are present.

Finally, as with all bedridden patients, attention should be given to maintaining adequate nutrition and muscle tone while preventing decubitus ulcers, contractures, thrombophlebitis and constipation. With proper supportive care, each botulism victim can expect complete neurologic recovery.

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